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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,774	12/21/2000	Christine A. Klein	50370-60637CDV	5116

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EXAMINER	
CHANDRA, GYAN	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,774	KLEIN ET AL.	
	Examiner	Art Unit	
	Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,8,17,25-27,36,37,39,50,51,53,77 and 78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5, 8-1 1, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/19/2004 has been entered.

Applicants' amendment filed on October 19, 2004 has been entered in full. Claims 1, 2, 5, 8, 9-11, 17, 25, 26, 39, 50, 51 and 53 have been amended. Claims 77-78 have been added. Claims 1, 2, 5, 8-1 1, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 are pending and under consideration.

The text of those sections of Title 35, U.S. code not included in this action can be found in a prior Office Action.

Supplemental Information Disclosure Statement

Applicants' Supplemental Information Disclosure Statement on 19 October 2004 has been made of record.

Claim Rejections - 35 USC § 101

The rejection of claims 1, 2, 5, 8-1 1, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 under 35 USC § 101 is maintained for the reasons of record. Applicants' arguments

have been fully considered but are not persuasive. The claimed invention is drawn to a mixture of recombinant yeast cells comprising a recombinant heterologous orphan G protein coupled receptor, wherein the receptor is expressed on the cell membrane and a recombinant gene encoding a heterologous test peptide, wherein the test peptide is transported to a location allowing interaction with the receptor expressed on the cell membrane.

Applicant argues that the yeast cells of the present invention are useful as a research tool for screening assays to identify compounds that modulate signal transduction activity through orphan G protein coupled receptors. Applicants further argue that the claimed yeast cells are useful to identify a ligand that modulates the signal transduction activity of the orphan receptor, regardless of the ultimate biological function of the orphan receptor. However, as was set forth in Brenner v. Manson, 383 U.S. 519 (1966), the instant invention lacks a specific and substantial real world utility absent elucidation of the biological function of the orphan receptor and any role that the ligands identified as modulators of the receptor would play in modulation or identification of any disease state associated with that biological function. Without further research and experimentation, the claimed yeast cells do not provide an immediate benefit to the public. The biological research contemplated using applicants' yeast cells is to take place sometime in the future, only after elucidation of the biological role of the orphan receptor. Any benefit to the public is speculative, at best.

Applicant further argues that labeling an invention as a "research tool" is not sufficient measure to reject under 35 USC § 101. As is specifically set forth in the utility

guidelines, however, research tools are useful only where they can be used in conjunction with other method steps to evaluate materials other than themselves or to arrive at some result. The claimed yeast cells comprising a gene encoding an orphan G protein coupled receptor are not research tools in this sense. Rather, they are themselves the subject of basic research. The usefulness or lack thereof of the subject of basic orphan G protein coupled receptor is yet to be established. In the absence of any data as to the receptor's biological function, there is no basis upon which to base a specific or substantial utility for the claimed yeast cells comprising a gene encoding the receptor.

Applicant argues that the goal of the invention is not to discern the biological function of the orphan receptor, but rather to identify a ligand that modulates the signal transduction activity of the orphan receptor. However, this asserted goal is in actuality nothing more than basic research to evaluate the possible biological role of the orphan receptor itself and as such, does not meet the standard for a specific and substantial real world utility which provides an immediate benefit to the public.

Applicants claim that the identification of a ligand of an orphan receptor is certainly "some identifiable benefit". Applicants cite examples of excerpts from PharmaVitae 2003 (Datamonitor) of Takeda Pharmacutical Corporation and its goal on searching orphan receptors with unknown ligands using genomic database; Fujusawa pharmaceutical Company with interest in discovering chemical compounds modulating orphan G protein-coupled receptors using Arena's constitutively activated Receptor Technology (CART) (attached Appendix A). Applicants state in their remarks that CART

is different and use genome data to identify an orphan receptor and establish a function of the receptor by using a technology different than disclosed in the instant application.

Applicants' argument has been fully considered, but is not deemed persuasive because a research tool can have commercial value as presented by Applicants in their remarks. CART technology creates a number of mutations/changes within a given gene so that one can achieve a constitutive active state of the protein/polypeptide. The instant invention of recombinant yeast cells comprising a recombinant orphan G protein coupled receptor and a recombinant heterologous polypeptide is a basic research tool to identify a possible peptide ligand that binds to a receptor, and is not a direct mean of associating on orphan G protein coupled receptor to a relevant biological function of the receptor. Orphan receptors have been conserved in evolution and are distributed through out the body like other known receptors, and are therefore, clearly involved in human biological functions. However, identification of specific biological function and disease association of an orphan receptor remains to be a basic research. Further, commercial success of any product depends on many factors other than utility e.g., marketing, less competition with other products or need for basic research to identify biological function and disease association of orphan receptors. Basic research using orphan receptors to study themselves does not meet the standard for utility.

Claim Rejections - 35 USC § 112, First Paragraph

The rejection of claims 1, 2, 5, 8-1 1, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 under 35 USC § 112, first paragraph, as lacking enablement, is maintained.

Applicants' argue that they have amended the claims to recite recombinant yeast cells comprising heterologous orphan G protein-coupled receptors. Thus, they claim that the claims as read in the light of examples 9 and 10, are enabled.

The statute 35 U.S.C. 112 requires that:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants' disclosure provides guidance as to how to prepare a random peptide library and how to prepare a mixture of yeast cells comprising a FPRL1 G protein receptor. Applicants' disclosure teaches how to identify a peptide that activates the pheromone response pathway in yeast expressing the FPRL1 receptor (Example 9) or the monocyte derived receptor 15 (MDR-15) (Example 10). However, applicants' disclosure does not disclose any specific peptide or peptide that is a ligand of MDR-15. While Applicants' disclosure shows how an orphan receptor can be used to screen a library of peptides to find a ligand, it does not provide sufficient guidance to enable one of skill in the art to be able to use the claimed yeast cells or the receptor ligand for any diagnostic or therapeutic purpose without undue experimentation.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 2, 5, 8-1 1, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 under 35 USC 103(a) as being unpatentable over King et al. (Science 250:121-123, October 5, 1990) in view of Devlin et al. (Science 249:404-406, July 27, 1990), Scott et al.

(Science 249:386-390, July 27, 1990), Cwirla et al. (Proc. Natl. Acad. Sci. USA, 87: 6378-6382, 1990), and Ladner et al. (U. S. Patent No. 5,096,815, March 17, 1992), as set forth in the previous office action (Paper No. 20, May 27, 2003), is maintained for the reasons of record. Applicants' arguments have been fully considered but they are not persuasive.

Applicants argue that the combination of King et al. with Develin/Scott/Cwirla would not have enabled one skilled in the art to express GPCR on a yeast cell membrane. However, King et al., do teach modification of NH2-terminal of hβ-AR gene for expression in the cell membrane of yeast (see page 121, 1st paragraph and the 4th line of the middle paragraph). They teach that a high level expression of the human β2-aderenergic receptor (hβ-AR) in yeast is achieved when the hβ-AR gene modified at NH2-terminal is placed under the galactose-inducible GAL1 promoter (page 121, left column, second paragraph).

Applicants argue that Ladner et al. teach away from the practice of using yeast cells as the host cell for intracellular library expression. However, Ladner et al. teach that though the preliminary experiments can be carried out in bacterial cells, the decisive experiments should be carried out in eukaryotic cells such as yeast or Chinese hamster ovary (CHO), this would result in correlating data for eukaryotic system in higher success rate (column 22, line 46-50). Therefore, Ladner et.al. do not teach that yeast cells cannot be used. Furthermore, King et al. teach making fusion proteins and use of fusion protiens to express in cell membrane of yeast. King et al. clearly state the

benefit of the yeast system for studying the ligand binding to G protein coupled receptors (page 121, end of the abstract). This would have motivated one of skill in the art at the time invention was made to have constructed a library of test peptides as taught by Delvlin/Scott/Cwirla/Ladner and produced a mixture of recombinant yeast cells by expressing a recombinant heterologous orphan G protein coupled receptor in the yeast cell membrane as taught by King et al.

Applicants argue that the Ladner et al. system does not use a random peptide library. However, the teachings of constructing a random peptide libraries are recited on page 387, 2nd paragraph of Scott and Smith, on page 404, 2nd paragraph of the middle column of Devlin et al. and on page 6378 and 3rd paragraph of the right column of Cwirla et al. Thus, the combined teachings of the references teach making a random peptide library and modification of a fusion peptide library for express and use within a cell, on a cell surface or in the cell membrane.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gyan Chandra
AU 1646
24 November 2004

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